REMARKS

Claims 34, 35 and 44 have been amended to delete the "same primers" language, to change "control sequence" to "at least one reference RNA sequence" and to specify the group of reference RNA sequences. Support for the types of reference RNA sequences can be found, for example, in claim 18 as originally filed and at page 6, lines 19-25 of the specification. Support for distinguishing the amplified target viral RNA sequence and amplified reference RNA sequence by size or by hybridization probes can be found at page 6, lines 28-30 and page 7, lines 20-27. Claims 38 and 39 have been amended to change the term "maxigene" to a reference RNA sequence which comprises target viral RNA sequence and non-target viral RNA sequence. An example of non-target viral RNA is an insert in the target viral RNA sequence.

New claims 50-113 have been added. Support for these new claims can be found throughout the application as filed. For example, support for new claims 50-52 can be found in original claim 27, page 6, lines 28-29, page 7, lines 6-10 and page 10, lines 24-29. Support for new claims 53-55 can be found in original claim 27, page 6, lines 19-21, page 6, lines 28-29, page 7, lines 6-10, page 7, lines 15-19 and page 10, lines 24-29. Support for new claims 56-113 can be found in original claim 27, page 6, lines 19-21, page 6, lines 28-29, page 7, lines 1-22 and page 10, lines 24-29.

It is submitted that the amendments of claims 34, 35, 38, 39 and 44 and new claims 50-113 do not constitute new matter and their entry is requested.

Applicants further submit that the amendments to claims 34, 35, 38, 39 and 44 and new claims 50-113 are fully supported by, at least, parent application, Serial No. 07/148,959 filed on 27 January 1988 (parent '959 application), particularly with respect to the quantitation of a target viral RNA using a reference RNA sequence as an internal control with simultaneous amplification. Each of the enumerated reference RNA sequences are disclosed in this parent application, with the exception of the reference RNA sequence with a deletion in the target viral RNA sequence.

The present invention is directed to a method for the quantitation of target viral RNA in a sample by simultaneously amplifying a target viral RNA sequence and a predetermined quantity of

a reference RNA sequence as an internal standard. That is, the target viral RNA sequence, if present, and the reference sequence are simultaneously amplified in the same reaction mixture. The quantity of target viral RNA present in the sample is determined by comparing the amount of the amplified target viral RNA and the amount of the amplified reference RNA based on the predetermined amount of reference RNA added as an internal control. The reference RNA sequence may be (i) a reference RNA sequence which does not comprise the target viral RNA sequence, (ii) a reference RNA sequence which comprises the target viral RNA sequence and has substantially more nucleotides than the target viral RNA sequence, (iii) a reference RNA sequence which comprises the target viral RNA sequence with at least about 20 nucleotides less than the target viral RNA sequence or (iv) a reference RNA sequence which comprises target viral RNA sequence and non-target viral-RNA sequence.

Applicants submit that none of the prior art previously cited in the prosecution of this application describe or suggest the claimed quantitation method. For example, Mullis et al. (US 4,683,195) does not describe or suggest the quantitation of a target viral RNA in a sample, does not describe or suggest the use of an internal control in a quantitation method and does not describe or suggest the use of a predetermined quantity of a reference RNA sequence as the internal control in a quantitation method. Similarly, Ratner et al. (*Nature* **313**:277-284, 1985), Hennighausen et al. (*EMBO J* **5**:1367-1371, 1986) and Wathen et al. (*J Virology* **41**:462-477, 1982) do not describe or suggest the quantitation of a target viral RNA in a sample, do not describe or suggest the use of an internal control in a quantitation method and do not describe or suggest the use of a predetermined quantity of a reference RNA sequence as the internal control in a quantitation method. The combination of Mullis et al. and any of Ratner et al., Hennighausen et al. and Wathen et al. also does not describe or suggest the quantitation of a target viral RNA in a sample, does not describe or suggest the use of an internal control in a quantitation method and does not describe or suggest the use of a predetermined quantity of a reference RNA sequence as the internal control in a quantitation method.

In addition, Applicants submit that the present claims are patentable over Rossi (US 5,622,820) and Cantin et al. (US 5,110,802). Specifically, Rossi issued from U.S. application Serial No. 08/334,398 filed on November 3, 1994 as a continuation application of U.S. application Serial No. 07/180,740 filed on April 12, 1988. The latter application was a continuation-in-part of U.S. application Serial No. 07/165,915 filed on March 10, 1988. Thus, the earliest effective filing date for Rossi is either April 12, 1988 or March 10, 1988, both of which are after the filing date of the parent '959 application.

Cantin et al. issued from U.S. patent application Serial No. 07/073,189 filed on July 14, 1987. Cantin et al. discloses the simultaneous PCR amplification of a target viral RNA sequence and a fixed concentration of a reference sequence with an insert between the primer sites of the target sequence (column 4, lines 45-53). Cantin et al. further discloses that the initial amount of reference sequence template remains constant thereby enabling one to determine the ratio of amplification of the reference sequence template versus the sample template before and after treatment to determine the effect of treatment on viral RNA synthesis (column 4, lines 57-60 and lines 44-45). The subject matter of the claims of the present application, which is not claimed in Cantin et al, was the invention of Murakawa, Wallace, Zaia and Rossi, the inventors of the present application involved and not the invention of Cantin. See Declaration of John J. Rossi, Ph.D. that was filed as Exhibit MX 1021 in Interference No. 105,055 (copy attached hereto).

Applicants also submit that the claims are patentable over the claims awarded to Wang in Interference No. 105,055 in view of the Board's decision that proposed claim 50 submitted, but not entered, during the interference was not directed to the same patentable invention as the Wang claims in view of the reference RNA sequence specified in proposed claim 50. Claim 50 submitted in the present amendment is similar to proposed claim 50, except that the language of the claim has been clarified. Claims 51-52 are dependent on claim 50. New claims 53-94 and 98-104 also contain specific language concerning the reference RNA sequence. Similarly, amended claims 34, 35, 38, 39 and 44 also contain specific language concerning the reference RNA sequence. Claims 95-97 and

105-113 are generic with respect to the reference RNA sequence in that it is distinguishable from the target viral RNA sequence by size or by hybridization probes.

In view of the above remarks, it is submitted that the claims are fully supported by the instant application and are patentable over the prior art of record. Reconsideration of this application and early notice of allowance is requested. The Examiner is invited to telephone the undersigned if it will assist in expediting the prosecution and allowance of the instant application.

Respectfully submitted,

ROTHWELL, FIGG, ERNST & MANBECK, p.c.

By _____

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Attachment: Copy of Rossi Declaration filed as Exhibit MX 1021 in Interference No. 105,055

2124-154 amendment 129.wpd

Filed on behalf of: Senior Party Murakawa et al.

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES
(Administrative Patent Judge Carol A. Spiegel)

ALICE M. WANG, MICHAEL E. DOYLE
and DAVID F. MARK

Junior Party,
U.S. Patent 5,219,727
U.S. Patent 5,476,774

v.

GEORGE J. MURAKAWA, R. BRUCE WALLACE,
JOHN A. ZAIA and JOHN J. ROSSI

Senior Party,
Application 07/402,450.

Patent Interference No. 105,055

DECLARATION OF JOHN J. ROSSI, Ph.D.

Murakawa EXHIBIT 1021
Wang v. Murakawa
Interference No. 105,055

I, John J. Rossi, Ph.D., declare as follows:

1. I am a joint inventor of Murakawa et al., U.S. patent application Serial No. 07/402,450 involved in the present interference ("the '450 application"). The other joint inventors of the Murakawa '450 application are George J. Murakawa, R. Bruce Wallace and John A. Zaia.

2. I am a joint inventor of Cantin et al., U.S. Patent No. 5,110,802 ("the '802 patent"). The other joint inventors of the '802 patent are Edouard M. Cantin, R. Bruce Wallace and John A. Zaia.

3. I believe that I, along with George J. Murakawa, R. Bruce Wallace and John A. Zaia, am an original, first and joint inventor of the subject matter described and claimed in the '450 application, and of the subject matter disclosed in column 4, lines 45-60 of the '802 patent, specifically the simultaneous amplification of a target viral RNA sequence that may be present in a sample and a reference RNA sequence in which the reference RNA sequence differs in length between the primer sites of the target sequence for the quantitation of the target viral RNA sequence.

4. I believe that I, along with Edouard M. Cantin, R. Bruce Wallace and John A. Zaia, am an original, first and joint inventor of the subject matter described and claimed in the '802 patent, specifically oligodeoxyribonucleotide methylphosphonates modeled as HIV antisense and its use for inhibiting HIV RNA synthesis.

5. The description at column 4, lines 45-60 of the '802 patent originated with the joint inventors of the '450 application.

6. Edouard M. Cantin did not make any inventive contribution to the subject matter described and claimed in the '450 application or the subject matter described at column 4, lines 45-60 of the '802 patent,

7. I declare further that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false testimony may jeopardize the validity of the Murakawa application or any patent resulting thereon.

Nov. 13, 2001

Date

John J. Rossi, Ph.D.